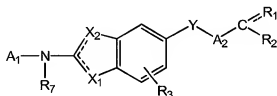


AMENDMENTS TO THE CLAIMS

1-74. (Canceled)

75. (Currently amended) A method of inhibiting Raf kinase activity in a human or animal subject suffering from a Ras/mitogen-activated protein kinase signal pathway-mediated cancer disorder selected from the group consisting of melanoma, breast cancer, prostate cancer, lung cancer, pancreatic cancer, thyroid cancer, bladder cancer, colon cancer, liver cancer, myeloid leukemia, and villous colon adenoma, comprising administering to the human or animal subject a composition comprising an amount of a compound of the formula (I) effective to inhibit Raf kinase activity in the human or animal subject:



(I)

wherein, X_1 and X_2 are $=N-$ or $-NR_4-$, provided that if X_1 is $-NR_4-$, then X_2 is $=N-$, or if X_2 is $-NR_4-$, then $[[X_2]] \underline{X_1}$ is $=N-$;

Y is O or S;

A_1 is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;

A_2 is substituted or unsubstituted heteroaryl;

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R₁ is O or H, and R₂ is NR₅R₆ or hydroxyl; or R₁ is taken together with R₂ to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;

R₃ is hydrogen, halogen, loweralkyl, or loweralkoxy;

R₄ is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl;

R₅ and R₆ are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkylalkylheterocyclo, and heteroarylalkyl; or R₅ and R₆ are taken together to form substituted or unsubstituted heterocyclo or heteroaryl; and

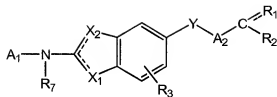
R₇ is hydrogen or loweralkyl;

or a pharmaceutically acceptable salt, ~~ester or prodrug~~ thereof.

76. (Previously presented) The method of claim 75 which further comprises administering to the human or animal subject at least one additional agent for the treatment of cancer selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

77. (Canceled)

78. (Currently amended) A method of inhibiting Raf kinase activity in a human or animal subject suffering from a Ras/mitogen-activated protein kinase signal pathway-mediated hormone dependent cancer disorder selected from the group consisting of breast cancer and prostate cancer, comprising administering to the human or animal subject a composition comprising an amount of a compound of the formula (I) effective to inhibit Raf kinase activity in the human or animal subject:



wherein, X_1 and X_2 are $=N-$ or $-NR_4-$, provided that if X_1 is $-NR_4-$, then X_2 is $=N-$, or if X_2 is $-NR_4-$, then $[[X_2]] \underline{X}_1$ is $=N-$;

Y is O or S;

A_1 is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;

A_2 is substituted or unsubstituted heteroaryl;

R_1 is O or H, and R_2 is NR_5R_6 or hydroxyl; or R_1 is taken together with R_2 to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;

R_3 is hydrogen, halogen, loweralkyl, or loweralkoxy;

R_4 is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl;

R_5 and R_6 are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkyloxyalkylheterocyclo, and heteroarylalkyl; or R_5 and R_6 are taken together to form substituted or unsubstituted heterocyclo or heteroaryl; and

R_7 is hydrogen or loweralkyl;

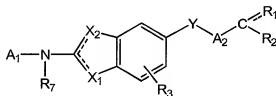
or a pharmaceutically acceptable salt, ~~ester or prodrug~~ thereof.

79. (Canceled)

80. (Previously presented) The method of claim 78 which further comprises administering to the human or animal subject at least one additional agent for the treatment of cancer selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

81. (Canceled)

82. (Currently amended) A method of inhibiting Raf kinase activity in a human or animal subject suffering from a Ras/mitogen-activated protein kinase signal pathway-mediated hematological cancer disorder, comprising administering to the human or animal subject a composition comprising an amount of a compound of the formula (I) effective to inhibit Raf kinase activity in the human or animal subject:



(I)

wherein, X_1 and X_2 are =N- or -NR₄-, provided that if X_1 is -NR₄-, then X_2 is =N-, or if X_2 is -NR₄-, then $[[X_2]] \underline{X}_1$ is =N-;

Y is O or S;

A₁ is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;

A₂ is substituted or unsubstituted heteroaryl;

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R₁ is O or H, and R₂ is NR₅ R₆ or hydroxyl; or R₁ is taken together with R₂ to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;

R₃ is hydrogen, halogen, loweralkyl, or loweralkoxy;

R₄ is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl;

R₅ and R₆ are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkyloxyalkylheterocyclo, and heteroarylalkyl; or R₅ and R₆ are taken together to form substituted or unsubstituted heterocyclo or heteroaryl; and

R₇ is hydrogen or loweralkyl;

or a pharmaceutically acceptable salt, ~~ester or prodrug~~ thereof.

83. (Previously presented) The method of claim 82 which further comprises administering to the human or animal subject at least one additional agent for the treatment of cancer selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

84-86. (Canceled)

87. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein X₁ is NR₄ and X₂ is N in formula (I).

88. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R₄ in formula (I) is hydrogen or C₁₋₆ alkyl.

89. (Previously presented) The method of claim 88, wherein R₄ in formula (I) is methyl.

90. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein Y in formula (I) is O.

91. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein A₁ in formula (I) is substituted or unsubstituted C₃₋₁₄ aryl.

92. (Previously presented) The method of claim 91, wherein A₁ in formula (I) is selected from the group consisting of substituted or unsubstituted phenyl, pyridyl, pyrimidinyl, phenylalkyl, pyridylalkyl, pyrimidinylalkyl, heterocyclylcarbonylphenyl, heterocyclylphenyl, heterocyclylalkylphenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, dihalophenyl, nitrophenyl, 4-bromophenyl, 4-chlorophenyl, alkylbenzoate, alkoxyphenyl, dialkoxyphenyl, dialkylphenyl, trialkylphenyl, thiophene, thiophene-2-carboxylate, alkylthiophenyl, trifluoromethylphenyl, acetylphenyl, sulfamoylphenyl, biphenyl, cyclohexylphenyl, phenoxyphenyl, dialkylaminophenyl, alkylbromophenyl, alkylchlorophenyl, alkylfluorophenyl, trifluoromethylchlorophenyl, trifluoromethylbromophenyl, indenyl, 2,3-dihydroindenyl, tetralinyl, trifluorophenyl, (trifluoromethyl)thiophenyl, alkoxybiphenyl, morpholinyl, N-piperazinyl, N-morpholinylalkyl, piperazinylalkyl, cyclohexylalkyl, indolyl, 2,3-dihydroindolyl, 1-aceetyl-2,3-dihydroindolyl, cycloheptyl, bicyclo[2.2.1]hept-2-yl, hydroxyphenyl, hydroxyalkylphenyl, pyrrolidinyl, pyrrolidin-1-yl, pyrrolidin-1-ylalkyl, 4-amino(imino)methylphenyl, isoxazolyl, indazolyl, adamantyl, bicyclohexyl, quinuclidinyl, imidazolyl, benzimidazolyl, imidazolylphenyl, phenylimidazolyl, phthalamido, naphthyl, benzophenone, aniliny, anisolyl, quinolinyl, quinolinonyl, phenylsulfonyl, phenylalkylsulfonyl, 9H-flouren-1-yl, piperidin-1-yl, piperidin-1-ylalkyl, cyclopropyl, cyclopropylalkyl, pyrimidin-5-

ylphenyl, quinolidinylphenyl, furanyl, furanylphenyl, N-methylpiperidin-4-yl, pyrrolidin-4-ylpyridinyl, 4-diazepan-1-yl, hydroxypyrrolidin-1-yl, dialkylaminopyrrolidin-1-yl, 1,4'-bipiperidin-1'-yl, and (1,4'-bipiperidin-1'-ylcarbonyl)phenyl.

93. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein A₁ in formula (I) is selected from the group consisting of substituted or unsubstituted phenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, dihalophenyl, nitrophenyl, 4-bromophenyl, 4-chlorophenyl, alkoxyphenyl, dialkoxyphenyl, dialkylphenyl, trialkylphenyl, alkylthiophenyl, trifluoromethylphenyl, acetylphenyl, sulfamoylphenyl, biphenyl, cyclohexylphenyl, phenoxyphenyl, dialkylaminophenyl, alkylbromophenyl, alkylchlorophenyl, alkylfluorophenyl, trifluoromethylchlorophenyl, trifluoromethylbromophenyl, trifluorophenyl, (trifluoromethyl)thiophenyl, alkoxybiphenyl, hydroxyphenyl, hydroxyalkylphenyl, 4-amino(imino)methylphenyl and (1,4'-bipiperidin-1'-ylcarbonyl)phenyl.

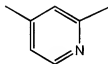
94. (Previously presented) The method of claim 93, wherein A₁ in formula (I) is 4-bromophenyl.

95. (Previously presented) The method of claim 93, wherein A₁ in formula (I) is trifluoromethylchlorophenyl.

96. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein A₂ in formula (I) is selected from the group consisting of substituted or unsubstituted phenyl, pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thiophenyl, furanyl, quinolinyl, purinyl, naphthyl, benzothiazolyl, benzopyridyl and benzoimidazolyl.

97. (Previously presented) The method of claim 96, wherein A₂ in formula (I) is pyridyl.

98. (Previously presented) The method of claim 96, wherein A₂ in formula (I) is



99. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R₁ is taken together with R₂ in formula (I) to form a substituted or unsubstituted C₃₋₈ heterocycloalkyl or C₃₋₁₄ heteroaryl group.

100. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R₁ is taken together with R₂ in formula (I) to form a group selected from substituted or unsubstituted phenyl, pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thiophenyl, furanyl, quinoliny, purinyl, naphthyl, benzothiazolyl, benzopyridyl and benzoimidazolyl.

101. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R₁ is taken together with R₂ in formula (I) to form a substituted or unsubstituted imidazolyl group.

102. (Previously presented) The method of claim 100, wherein the imidazolyl group is substituted with a halo C₁₋₆ alkyl group.

103. (Previously presented) The method of claim 100, wherein the imidazolyl group is substituted with a trifluoromethyl group.

104. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R_3 in formula (I) is hydrogen.

105. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R_4 in formula (I) is hydrogen.

106. (Previously presented) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R_5 and R_6 in formula (I) are independently selected from hydrogen and methyl.

107. (Canceled)

108. (Previously presented) The method of claim 75, wherein the cancer is melanoma.

109. (Previously presented) The method of claim 75, wherein the cancer is a carcinoma of the lungs, pancreas, thyroid, bladder or colon.

110. (Previously presented) The method of claim 75, wherein the cancer is myeloid leukemia.

111. (Previously presented) The method of claim 75, wherein the cancer is villous colon adenoma.

112. (Previously presented) The method of claim 82 wherein the hematological cancer disorder is chronic myelogenous leukemia.